UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,622	02/07/2002	Lieping Chen	07039-331001	3225

26191 7590 05/03/2005

FISH & RICHARDSON P.C.
PO BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
OUSPENSKI, ILIA I	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,622	CHEN ET AL.	
	Examiner	Art Unit	
	ILIA OUSPENSKI	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *8-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of Refererences Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *06/05/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims1 – 23 are pending.

2. Applicant's election without traverse of Group I (Claims 1 – 7, drawn to a purified mutant ICOS polypeptide) in the reply filed on 08/30/2004 is acknowledged. Applicant further elects the Species of the amino acid substitution Ser76Glu.

In the interest of compact prosecution, the prior art search has been extended to include the Species of the amino acid substitution Lys52Ser.

3. Claims8 – 23 are withdrawn from further consideration by the Examiner, under 37 C.F.R. § 1.142(b), as being drawn to nonelected inventions.

Claims 1 – 7 are under consideration in the instant application.

4. Applicant's IDS, filed 06/05/2002, is acknowledged, and has been considered.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code, e.g. on page 6, first paragraph. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1 – 7 are rejected under **35 U.S.C. 112, second paragraph,** as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 – 7 are indefinite in the recitation of "B7-H2" because its identity is unclear. The natural ligand for ICOS is known at least as B7h, B7RP-1, GL50, and LICOS, in addition to B7-H2 (e.g. as reviewed by Wang et al., J. Exp. Med., 2002, 8: 1033 – 1041; see page 1033 right column). Furthermore, the name B7-H2 is also used to designate a different B7-related protein (e.g. Coyle et al., US Patent No. 6,630,575; see e.g. Summary of Invention at columns 3 – 4). Therefore, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Amending the claims to recite the appropriate SEQ ID Number would obviate this rejection.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1 – 3, 5, and 7 are rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for an ICOS polypeptide which differs from SEQ ID NO:12 by the specific amino acid substitutions recited in claims 4 and 6, does not reasonably provide enablement for the broadly recited genus of "ICOS polypeptide." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification discloses on page 5 that an "ICOS polypeptide" is any polypeptide that is at least 5 amino acids in length, and has an amino acid sequence that is the same as, or substantially homologous to, the corresponding portion of the wild-type ICOS protein having the amino acid sequence of SEQ ID NO:12. The "substantially homologous" ICOS polypeptide is defined as having amino acid sequence that is at least 75% homologous to the corresponding portion of the wild type ICOS of SEQ ID NO:12 (pages 5 – 6 bridging paragraph).

Therefore, the instant claim recitation of a "purified ICOS polypeptide" reads on a genus of polypeptides that are

(A) at least 75% homologous to SEQ ID NO:12, and

(B) fragments of such polypeptides.

The specification does not provide a sufficient enabling description of the claimed invention, for the reasons set forth herein.

(A) Percent identity.

The claims are directed to a genus of nucleotide sequences encoding polypeptides having at least 75% identity to a reference sequence, and require that the encoded polypeptides share a functional activity, namely having affinity for B7-H2 which is at least 6% of the affinity of wild-type ICOS polypeptide. Applicant has disclosed five nucleic acid variants encoding mutant ICOS polypeptides consistent with the functional requirements recited in the claims. However, in the absence of some structural basis for that function that must be maintained by the members of the genus, the claimed invention is not described in such a way as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention.

Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Finally, even single amino acid differences can result in drastically altered functions between two costimulatory proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability, the skilled artisan would not reasonably expect a polypeptide having 75% to SEQ ID NO:12 to share the same function as the polypeptide of SEQ ID NO:12, because there is insufficient guidance to direct the skilled artisan as to those essential sequences for the disclosed activities.

Thus the recitation of percent identity language does not allow the skilled artisan to make and use the encoding nucleic acids commensurate in scope with the instant claims without undue experimentation.

(B) Fragments.

The instant claims, when read in light of the specification, encompass fragments of at least five amino acids of SEQ ID NO:12, or fragments at least 75% identical to SEQ ID NO:12, and require that the fragments share a functional activity, namely having affinity for B7-H2 which is at least 6% of the affinity of wild-type ICOS polypeptide.

However, the specification does not appear to have provided sufficient guidance as to which fragments of SEQ ID NO:2 would share the functional activity of having affinity for B7-H2 which is at least 6% of the affinity of wild-type ICOS polypeptide. Neither does the specification appear to have provided any working examples of any functional fragments. Thus it would require undue experimentation of the skilled artisan to determine which subsequences of SEQ ID NO:12 would have the function of the full length molecule, and in turn identify nucleic acid subsequences which encode these subsequences. Thus the teachings set forth in the specification provide no more than a plan or invitation for those skilled in the art to experiment practicing the claimed invention.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. Claims 1 – 7 are rejected under **35 U.S.C. 112, first paragraph**, because the specification, while being enabling for an ICOS polypeptide of specified sequence having altered affinity for B7-H2 compared to wild-type ICOS polypeptide of SEQ ID NO:12, does not reasonably provide enablement for an ICOS polypeptide of specified sequence having altered affinity for B7-H2 compared to "**a** wild-type ICOS polypeptide," as generically recited by the instant claim language. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not provide a sufficient enabling description of the claimed invention.

It is noted that the specification appears to define "wild-type ICOS" as a protein "having" the amino acid sequence of SEQ ID NO:12 (page 5 lines 21 – 22). The transitional phrase "having" is interpreted as open language, i.e. meaning that the scope of "wild-type ICOS" is not limited to SEQ ID NO:12. This interpretation in the context of the instant claims appears to be supported by the language of claims 1 and 2, wherein the dependent claim 2 "further limits" the sequence of "wild-type ICOS" to SEQ ID NO:12.

Applicant is invited to clarify the record with regard to the intended scope of the recitation "wild-type ICOS." Alternatively, Applicant is invited to amend claim 1 to recite wild-type ICOS polypeptide of SEQ ID NO:12.

The term "having" is open-ended and extends the sequence to include additional undisclosed sequences on either or both sides of the disclosed region. There is insufficient guidance in the specification as filed to direct a skilled artisan to the lengths or nature of such additional sequences which would result in binding affinities recited in the claims. In view of the unpredictability of the art, as discusses in the references cited in section 9 above, a person of skill in the art would not be able to determine without undue experimentation which of the plethora of sequences encompassed by the instant claims would share the ability to bind to B7-H2, other than the wild-type ICOS polypeptide of SEQ ID NO:12.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary, the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

12. Claims 1, 2, and 7 are rejected under **35 U.S.C. 102(b)** as being anticipated by Ling et al. (US Patent No. 6,521,749; see entire document).

It is noted that the instant claim recitation of an "ICOS polypeptide," interpreted in light of the specification on pages 5 – 6, reads on a genus of polypeptides that are (a) at least 75% homologous to SEQ ID NO:12, and (b) fragments of such polypeptides that are at least five amino acids in length.

Ling et al. teach a polypeptide of SEQ ID NO:24 (human ICOS-IgG fusion protein), which is identical to the instantly claimed SEQ ID NO:12 over 120 amino acids. Ling et al. further teach that ICOS binds to GL50 (an alternate name for the instantly claimed B7-H2). Since Ling et al. teach the same protein as instantly claimed, its functional properties, such as affinity to B7-H2/GL50, or ability to inhibit T cell activation, are inherently the same.

Thus the reference teachings anticipate the instant claimed invention.

13. Claims 1 and 7 are rejected under **35 U.S.C. 102(e)** as being anticipated by Tamatani et al. (US Pat. Pub. 2002/0156242).

Tamatani et al. teach a purified "JTT-1 antigen," (SEQ ID NO:2) which is identical in sequence to the instantly claimed ICOS polypeptide of SEQ ID NO:12. Since the polypeptide taught by Tamatani et al. is the same as instantly claimed, it inherently possesses the same ability to inhibit T cell activation in a T cell proliferation assay as the instantly claimed ICOS polypeptide.

Thus the reference teachings anticipate the instant claimed invention.

14. Conclusion: No claim is allowed.

Claims 4 and 6 appear to be free of prior art.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ILIA OUSPENSKI whose telephone number is 571-272-2920. The examiner can normally be reached on Monday-Friday 9 - 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ILIA OUSPENSKI
Patent Examiner
Art Unit 1644

April 27, 2005

PHILLIP GAMBEL, PH.D
PRIMARY EXAMINER
TECH CENTER 1600
4/28/05